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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/989,721	11/19/2001	Avi J. Ashkenazi	P2730P1C55	2434

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EXAMINER

SPECTOR, LORRAINE

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/989,721

Applicant(s)

ASHKENAZI ET AL.

Examiner

Lorraine Spector, Ph.D.

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 119-138 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 119-138 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 November 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 5/24/02.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

Part III: Detailed Office Action

Claims 119-138 are pending and under consideration.

The claims are drawn to nucleic acids encoding PRO809, also identified as DNA57836-1338 and ATCC accession number 203025, shown in Figures 150 (nucleic acid) and 151 (protein).

Formal Matters:

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

IDS:

The information disclosure statement, filed 5/24/2002, has been considered. The BLAST results demonstrate that applicants are aware of nucleic acids with identity/homology to the one claimed herein. However, as the BLAST results do not give sufficient identifying information, the Examiner cannot determine if said sequences constitute prior art.

Priority Determination:

This invention is found to lack utility, see rejections below. Accordingly, priority is merited only to the instant filing date, 11/19/2001.

Should the applicant disagree with the examiner's factual determination above, it is incumbent upon the applicant to provide the serial number and specific page number(s) of any parent application filed prior to the date recited above which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of and fully enabled for prior to that date.

Objections and Rejections under 35 U.S.C. §§ 101 and 112:

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 119-138 are rejected under §35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility.

The specification discloses a protein designated PRO809, and nucleic acid encoding such. There is no discussion of the structure of the protein encoded by the claimed nucleic acids, nor disclosure of any relationship between such structure and a purported function. There is no disclosure of any disease or condition in any way related to the nucleic acids that are claimed, nor disclosure of any diagnostic or analytical assay that could be performed using the claimed nucleic acids.

The specification discloses that the claimed nucleic acids may be used as hybridization probes, to make antisense nucleic acids, and for the preparation of protein, to make transgenic animals, and in gene therapy. None of these assertions is specific, as none makes use of any specific property of the claimed nucleic acids, but rather could be asserted as a use for any nucleic acid that encodes any protein.

Utility must be in readily available form. In *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sup. Ct., 1966), a process of producing a novel compound that was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be useful because the compound produced thereby was potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The instant claims are drawn to a polynucleotide encoding a protein which has undetermined function or biological significance. Until some actual and specific activity can be attributed to the protein identified in the specification as PRO809 protein or the polynucleotides encoding it, the claimed invention is incomplete. Merely

using the polynucleotides to determine the properties of the encoded protein does not constitute a patentable utility.

It is further noted that PRO809 is disclosed as having given positive results in a single assay, Example 170 beginning at page 539 of the specification, a gene amplification assay. Therein, PRO809 was found to be amplified approximately two fold in 3 of 10 human lung tumor squamous cell carcinoma cell lines, 2 of 9 human lung tumor adenocarcinoma cell lines, and the sole human lung tumor large cell carcinoma cell line. The finding that the nucleic acid encoding PRO809 is amplified, likely indicating aneuploidy, in the aforementioned tumor types is insufficient to confer utility to the nucleic acid. Cancerous tissue is known to be aneuploid, that is, having an abnormal number of chromosomes (see Sen, 2000, Curr. Opin. Oncol. 12:82-88). The data presented in the specification were not corrected for aneuploidy. A slight amplification of a gene does not necessarily mean overexpression in a cancer tissue, but can merely be an indication that the cancer tissue is aneuploid. The preliminary data were not supported by analysis of mRNA or protein expression, for example. In this case, the sequence of PRO809 was found at no more than two copies per cell, and only in a minority of tumors tested. The person of ordinary skill in the art would not consider the results to be significant or diagnostic in view of the review by Sen.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 119-138 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 119-124, 127-128 and 132-138 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polynucleotides having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence, or that merely hybridize to a disclosed sequence. The claims do not require that the claimed polynucleotide encode a particular protein, nor that any protein encoded thereby possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polynucleotides that are defined only by sequence identity. Further, numerous of the claims define such in relation to the 'extracellular domain' of the protein, for which there is no description in the specification. The structure of the putative PRO809 peptide is only briefly discussed in the specification; there is no disclosure that the protein is expected to be a transmembrane protein, nor of any extracellular domain.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved

until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, nucleic acids comprising the sequence set forth in SEQ ID NO:222, degenerate variants thereof or fragments thereof sufficiently long to be used as hybridization probes but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 119-138 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims that recite "the extracellular domain" of the protein are indefinite as no extracellular domain has been described. Therefore, the metes and bounds of the claims cannot be determined. For example, see Claim 119, parts (c) and (d). Further, if the protein had an extracellular domain, the recitation of "the extracellular domain"..."lacking its associated signal sequence" (claim 119, part (d), for example) is indefinite as a signal sequence is not generally considered to be part of an extracellular domain, as signal sequences are cleaved from said domains in the process of secretion from the cell.

Claims that recite that the claimed nucleic acid "hybridizes to" another sequence, such as claim 132, are indefinite as there is no limiting definition of such in the specification, and the metes and bounds of that which will hybridize are dependent upon the conditions under which the hybridization is performed. As the metes and bounds of what will hybridize to a given sequence are entirely dependent upon the conditions of hybridization and washing, the metes and bounds of the claims cannot be determined. With respect to claim 133, although the further limitation that the hybridization conditions are "stringent" is introduced, the term "stringent conditions" is also a relative term, and the metes and bounds of the claim cannot be determined.

The remaining claims are rejected for depending from an indefinite claim.

Deposit requirement:

Claims 119-138 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The deposit of biological organisms is considered by the Examiner to be necessary for enablement of the current invention (see 37 C.F.R. §1.808(a)). Examiner acknowledges the deposit of organisms under accession number ATCC 203025 under terms of the Budapest Treaty on International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure in partial compliance with this requirement. However, in order to be fully compliant with the requirement, applicants must state that the deposit will be maintained for a term of at least 30 years *and at least five (5) years after the most recent request for the furnishing of a sample of the deposit was received by the depository*. See 37 C.F.R. §1.806.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 119-138 are rejected under 35 U.S.C. 102(b) as being anticipated by clone H74302, isolated by L. Hillier et al., WashUMerck EST Project 1995. By applicants admission at page 454 of the specification, the clone that was sequenced and designated DNA57836-1338 or PRO809, was purchased from Merck under clone designation H74302. According to NCBI, the cDNA was double stranded, and inserted in the "Lafmid BA vector", which was propagated in E. coli cells. With respect to claim 136, the DNA would necessarily have been "operably linked" to sequences in the vector for control of replication of the vector.

A search of commercial sequence databases revealed numerous sequences with identity to SEQ ID NO: 222. L. Hillier et al., WashUMerck EST Project 1995 in particular, disclosed via electronic media numerous sequences from a human cDNA library. The electronic disclosures state that the cDNA was double stranded, and inserted in the "Lafmid BA vector", which was propagated in E. coli cells. It is not clear whether this vector is or is not an expression vector. Among the sequences disclosed by Hillier et al. are:

Result *	Locus Number	Date	Percent identity	to bases x-y of SEQ ID NO: 222	% Identity relative to shorter sequence	regions of 100% identity
2	H74303	10/31/95	99.3	556-969	99.3	587-969
4	H73373	10/31/95	92	12-479	90	14-349
5	H58326	10/5/95	96.1	279-685	93.8	284-484, 486-593
11	RO2548	3/31/95	98.9	693-974	73.6	698-974

* See appended computer printout of sequence search results

Claims 119-123 and 132-138 are rejected under 35 U.S.C. 102(b) as being anticipated by L. Hillier et al., WashUMerck EST Project 1995. Specifically, claims 119-123 and 132-138 are rejected over locus H74303, claims 119-121 and 132-138 are rejected over locus H58326, claims 119-121 and 132-138 are rejected over locus H73373, and claims 132-134 are rejected over

locus RO2548. Although Hillier et al. do not have the entirety of SEQ ID NO: 222 in any single clone, the clones referenced above meet the limitations of the claims sequence identity is calculated relative to the shorter of two sequences being compared. Further, any of the Hillier sequences would hybridize to SEQ ID NO: 222 under "stringent" hybridization conditions. With respect to claim 136, the DNA would necessarily have been "operably linked" to sequences in the vector for control of replication of the vector. Therefore, the claims are anticipated by Hillier et al.

Advisory Information:

No claim is allowed.

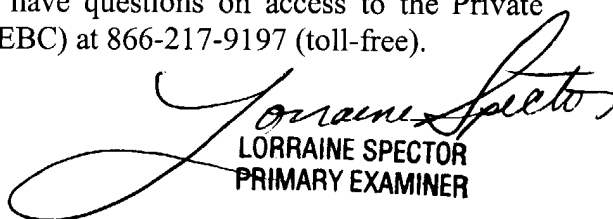
Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 3:00 P.M. ***Effective 1/21/2004, Dr. Spector's telephone number is 571-272-0893.***

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary L. Kunz. ***Effective 1/21/2004, Dr. Kunz' telephone number is 571-272-0887.***

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to ***571-273-0893.***

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


LORRAINE SPECTOR
PRIMARY EXAMINER